

24 August 1956

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MEMORANDUM FOR: THE RECORD

SUBJECT: Trip to Lexington, Ky., 21-23 August 1956

1. Dr. Isbell is obtaining supplies of acetyl LSD, 1-methyl LSD, BOL-148, and the pyrrolidide of LSD. He will check these compounds in his subjects for LSD-like reactions, for cross tolerance to LSD, and pay particular attention to time course of the action in each case and the odd reactions. I agreed to furnish what data we have on the pyrrolidide compound.
2. He will check the time course, potency and general effectiveness of the dispersed C-9 compound which I furnished in adequate supply. He is looking at the circulatory effects of the C materials in general. He has approximately 15 pounds of fresh Charas that he would like to give us. This would involve us seeing Mr. Cunningham in Anslinger's office, since Mr. Cunningham is responsible for the material.
3. Dr. Isbell provided me with one gram of 1-dromeran tartrate and 0.5 grams of the phenethyl derivative. The phenethyl derivative is 5 times more potent than 1-dromeran but in all other ways is strictly comparable in its action. It is the most potent of all morphine derivatives by far. Dr. Isbell has no doubt of its oral potency but is testing it. The ratio of intramuscular to oral potency is estimated to be 1.5 to 1. This particular substance probably will never be marketed by Hoffman La Roche because it offers no advantage except the greater potency and is more difficult to make. The antidote for the respiratory depression produced by the compound is Nalline. I queried Dr. Isbell on the possible use of 0.8 milligrams of this compound on our need for use against guards. He thought that very possibly the guard in a short time would be unable to perform his duty and might very possibly be unaware of his surroundings.
4. Dr. Isbell finds that the Rivea seeds given him by NIH produce neurological signs, mydriasis, etc., but also so much gastro-intestinal trouble (from the resins) that he can't evaluate any psychological effects. I explained to him the confusion between the two types of seeds and gave him an adequate sample of the larger seeds from the Mexican mainland for trial as he has time.

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I also indicated that as soon as it was available, I would send him an extract from which the resins have been removed.

5. Dr. Isbell has the compound 2,2-diphenyl-4-morpholino-ethyl butyrate (note: gamma amino butyrate) which can replace morphine in preventing abstinence symptoms but at the same time produces a rather acute toxic psychosis of two to three days' duration. More information will be available on this compound later.

6. I queried Dr. Isbell on the possible use of orinase to potentiate and/or prolong the LSD reaction (based on information that orinase lowers the capacity of the liver to perform its normal detoxifying function). He felt that a considerable amount of information could be gotten about the feasibility of this through some animal work with the compound prior to his human work. He suggested use of Dr. Winter's technique. If the animal work indicates that this is a feasible approach, he will be very glad to do the human work with the material.

7. Dr. Isbell is very interested in testing the French compound if we can furnish him with the substance and some animal data. His interest in the compound comes from its possible connection with the active compounds found in nutmeg, etc.

8. In connection with the problem of checking the effects of drugs on suggestibility, Dr. Isbell felt that a standard procedure could be worked out which would not necessarily require the use of a hypnotist. The technique he suggests consists of the production of a standard tape recording which suggests that a person is swaying on his feet. The subject is placed in a sway meter. There his tendency for normal swaying and swaying under suggestion will be measured at different times in order to determine reproducibility in the same individual. Later the drug is introduced to determine whether the subject is then more susceptible to the playing of the tape. We also discussed the problems of arriving at objective tests for depth of hypnosis. In relation to this, Dr. Isbell felt that it might be instructive first to apply whatever tests that we decide are germane to the problem to somnambulist subjects in states such as rigid suspension between chairs or complete anesthesia, etc., in order to eliminate as far as possible

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doubts as to the genuineness of the condition and to get as large a change in the subject as is possible.

9. Dr. Isbell suggested that the problem of an anti-interrogation material might be solved by the injection of between 30 and 60 milligrams of d, l acetyl methadol (alpha-d, l-4, 4 diphenyl-6-dimethylamino-3-acetoxy-heptane). The effect would be profound, not too dangerous and would follow the time course indicated below:

	<u>Effect Begins</u>	<u>Peak Effect</u>	<u>Mild Residual Effects</u>
1-	10-15 mins.	1 1/2 - 2 hrs.	24 hours
d-	3-4 hrs.	12 hours	72 hours

Nalline will only antidote the respiratory depression, not the analgesic effect, the emetic effect, nor the psychological effect. Therefore, it would be possible to keep the person alive in the event of an overdose by the use of Nalline, but it would not be possible to put him in a condition for interrogation.

10. Dr. Wikler has finished his review on the electro-physiology of the central nervous system and Dr. Isbell will send us a copy of the manuscript soon. Dr. Isbell will be in Washington part of the week of 20 September and will be glad to talk to us then.



Chief, Branch II
TSS/Chemical Division

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